

AMENDMENTS TO THE SPECIFICATION:

Please replace the paragraph beginning on page 2, line 27, and ending on page 3, line 5 with the following paragraph:

The chicken GHRH receptor has been cloned and functions similar to the natural source tissue (chicken pituitary cells) in that it ~~responding~~ responds to human GHRH but not to the reported chicken hormone. This led us to suspect a problem with the supposed chicken GHRH hormone. The chicken GHRH polypeptide was then recloned from freshly flash frozen chicken hypothalami and sequenced. The nucleic acid sequence of the newly isolated chicken GHRH gene did not agree with the published sequence and the synthesized chicken hormone based on this new sequence was found to be active at the cloned chicken GHRH receptor. The present invention is directed to the use of the new chicken GHRH hormone and its corresponding GHRH receptor to enhance the production of larger, leaner chickens and other avian species used for meat production.

Please replace the paragraph beginning on page 6, line 31, and ending on page 7, line 7 with the following paragraph:

The present invention is directed to the use of the chicken GHRH polypeptide and the chicken GHRH receptor to enhance the production of larger, leaner chickens and other avian species used for meat production and enhance feed utilization. In accordance with one embodiment, a chicken GHRH polypeptide, comprising the amino acid sequence of SEQ ID NO: 1 or a polypeptide that differs from SEQ ID NO: B 1 by one or more conservative amino acid substitutions yet retains its ability to ~~stimulating~~ stimulate second messenger signaling at the cloned

chicken GHRH receptor, is administered to an agriculturally significant avian species to enhance the growth of the avian species.

Please replace the paragraph beginning on page 7, line 8, and ending on page 7, line 19 with the following paragraph:

The sequence of a chicken GHRH polypeptide has been previously reported however that polypeptide has been tested in chickens and chicken pituitary cells, and had little or no GH releasing activity while human GHRH was found to be active. The present invention is directed to GHRH polypeptides that are capable of stimulating second messenger signaling at the chicken GHRH receptor comprising the sequence of SEQ ID NO:4. The nucleotide sequence of the chicken GHRH receptor gene, with the 5' and 3' untranslated region (start codon located at bp 54, stop codon located at bp 1312) is shown as SEQ ID NO:[1] 3. The coding sequence of chicken GHRH receptor is shown as SEQ ID NO: 6. In accordance with one embodiment of the present invention a chicken GHRH having the amino acid sequence of SEQ ID NO: 2 is provided. This sequence differs from the previously reported sequence at amino acid number 21, wherein the present sequence has a lysine and the previously reported sequence has an asparagines.

Please replace the paragraph beginning on page 7, line 20, and ending on page 8, line 2 with the following paragraph:

Synthesis of the chicken GHRH(1-33)NH₂, based on the nucleotide sequence of SEQ ID NO: 1, produced a polypeptide that is active in binding to chicken pituitary membranes and competes with human GHRH. At the recombinant

chicken GHRH receptor the new polypeptide is active in binding and in signaling through the second messenger cAMP. This new chicken polypeptide is thus a functional GHRH. While the new sequence is active, it is less potent at the chicken receptor than human GHRH. This may be inherent to chicken physiology, or it may be an artifact of the truncated polypeptide (1-33) that was tested. Only amino acids 1-29 are required for full GHRH activity in mammalian systems that have been tested. This may be different in other animals. Active fragments of the chicken GHRH are also within the scope of this invention, including but not limited to truncated polypeptides that include amino acid residues (1-33) and 1-29 of SEQ ID NO: 2, respectively. Thus, one aspect of the present invention relates to a substantially pure protein and biologically active fragments thereof having chicken growth hormone releasing hormone (GHRH) receptor activity.

Please replace the paragraph beginning on page 8, line 3, and ending on page 8, line 11 with the following paragraph:

The present invention also encompasses nucleic acid sequences that encode a peptide or polypeptide that binds to chicken GHRH receptor and is capable of signaling through the second messenger cAMP is provided. In one preferred embodiment the nucleic acid comprises the sequence of SEQ ID NO: 6 1. In one embodiment a transgenic avian species is provided wherein one or more of the chickens cells comprise a nucleic acid sequence encoding the chicken GHRH protein of SEQ ID NO: 2. Accordingly, the present invention provides for recombinant organisms and progeny thereof comprising an exogenous gene encoding for a chicken GHRH and biologically active fragments thereof.

Please replace the paragraph beginning on page 13, line 22, and ending on page 13, line 28 with the following paragraph:

Positive colonies were used to inoculate Luria broth containing ampicillin that was incubated overnight at 37° C in a shaker. The plasmid DNA was purified from the bacteria using a Quiaprep spin Mini-Prep Kit (Quiagen). A total of nine clones from two different PCR reactions were sequenced (both forward and backward) using an automated ABI dye sequencer, and all showed lysine at position 21. The resultant cDNA sequence is shown in SEQ ID NO: 1, and the encoded polypeptide in SEQ ID NO: 2.

Please replace the paragraph beginning on page 14, line 5, and ending on page 14, line 13 with the following paragraph:

The remaining RNA was used to perform RT-PCR reactions utilizing degenerate primers designed to detect all known GHRH receptor cDNAs. A short segment of cDNA was sequenced confirming that we were dealing with the GHRH receptor. Specific primers were designed from this sequence which were used to screen the cDNA library for a full length receptor cDNA clone. The resultant cDNA sequence for the ~~HGRH~~ GHRH receptor is shown in SEQ ID NO: 3, and the encoded polypeptide in SEQ ID NO: 4. (figures 3 & 4). The chicken cDNA sequence has less than 63% identity with the human GHRH receptor compared to 83 to 96% identity among known mammalian GHRH receptors.

Please replace the paragraph beginning on page 15, line 22, and ending on page 15, line 28 with the following paragraph:

The chicken GHRH receptor will also be used to identify GHRH analogs and mimetics that stimulate GH release in poultry. In accordance with one embodiment the nucleic acid sequence of SEQ ID NO: 3 or SEQ ID NO: 6 is used as a probe to isolate related genes from chicken and other avian species. This could be important agriculturally for the improvement of feed utilization and the efficient production of larger, leaner chickens and other avian species used for meat production.